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SENNIGER POWERS LLP 100 NORTH BROADWAY 17TH FLOOR ST LOUIS, MO 63102				
EXAMINER				
NIGIN, RUSSELL SCOTT				
ART UNIT		PAPER NUMBER		
1631				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

uspatents@senniger.com

### Office Action Summary

**Application No.**

10/533,479

**Applicant(s)**

KARLSEN ET AL.

**Examiner**

RUSSELL S. NEGIN

**Art Unit**

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**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 16 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 40-77 is/are pending in the application.
- 4a) Of the above claim(s) 41 and 55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 40, 42-54 and 56-77 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SI/08)
- Paper No(s)/Mail Date 1/16/09
- 4) ☐ Interview Summary (PTO-413)
- Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Comments***

Claims 41 and 55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12 February 2008.

Applicants' amendments and request for reconsideration in the communication filed on 16 January 2009 are acknowledged and the amendments are entered.

Consequently, claims 40-77 are pending in the instant application; claims 40, 42-54, and 56-77 are examined in the instant Office action.

### ***Information disclosure statement***

The information disclosure statement filed on 16 January 2009 has been considered.

### ***Priority***

Applicant's arguments regarding priority are persuasive (see page 9 of the Remarks). The priority date of the instant application is 1 November 2002.

***Specification***

The objection to the specification is withdrawn in view of arguments filed on page 9 of the Remarks of 16 January 2009.

***Withdrawn Rejections***

The rejection of claim 44 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of amendments filed to the instant set of claims on 16 January 2009.

The rejection of claim 63 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of arguments filed on page 9 of the Remarks of 16 January 2009.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

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the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The following rejection is reiterated and is necessitated by amendment for instant claim 76:

35 U.S.C. 103 Rejection #1:

Claims 40, 43-50, 56-63, 69, 71-74, and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodey et al. [Journal of the American Chemical Society, volume 123, 2001, pages 2559-2570] in view of Fogler [Elements of Chemical Reaction Engineering, 2<sup>nd</sup> edition, New Jersey: Prentice Hall, 1992, pages 270-273] in view of Costa et al. [US Patent 5,545,529; issued 13 August 1996, filed 27 March 1995] in view of Levesque et al. [Journal of Biomechanical Engineering, 1985, volume 107, pages 341-347].

Claim 40 is drawn to a microfabricated device for fragmenting nucleic acids present in a fluid sample, the device comprising an inlet port, a fragmentation cell, and an outlet port downstream from said inlet port, said cell being in fluid communication with said ports, and wherein said outlet port is dimensioned to impede the flow of a fluid sample out of said cell so as to effect shearing of nucleic acid molecules therein,

wherein the fragmentation cell comprises a chamber having a bottom wall being generally perpendicular to the direction of flow of fluid through the outlet port, and wherein the fragmentation cell has a top wall in which the inlet port is formed, and side walls which extend from the top wall to the bottom wall, and wherein the side walls taper inwardly to meet the inlet port.

The article of Goodey et al. studies the development of multianalyte sensor arrays composed of chemically derivatized polymeric microspheres localized in micromachined cavities. Specifically, Figure 2 on page 2563 illustrates the microfabricated device of interest. The device has an inlet port and an outlet port separated by a chamber in communication with both ports. The outlet port, as illustrated in Figures 1-2 on page 2563 of Goodey et al., is in the bottom wall of the chamber and is dimensioned to impede the flow through the chamber. This bottom wall, as illustrated in Figure 2B of Goodey et al. is perpendicular to the flow of liquid in the chamber. The inlet port is in the top portion of the chamber, and Figure 2 of Goodey et al. illustrates side walls extending to the bottom of the chamber.

However, Goodey et al. does not show tapering of the side walls to meet the input port or use of the device to shear oligonucleotides.

The text of Fogler reviews many types of chemical reactors. Specifically, page 272 of Fogler illustrates in Figure 6-16, a reactor in which the walls of the reactor taper to meet the input port.

However, Goodey et al. and Fogler do not show use of the reactors to shear oligonucleotides.

The article of Levesque et al. studies the shearing of cultured endothelial cells, and illustrates the shearing apparatus in Figure 1 on page 341. This same mechanical shearing principle (as applied to cells in Levesque et al.) also applies to oligonucleotides as illustrated in the cover figure of Costa et al., which assays the result nucleotides for detecting the presence of complexes.

Claim 43 is further limiting wherein the width of the fragmentation cell abruptly decreases.

Claim 44 is further limiting wherein the dimensions of this constriction are recited.

Claim 45 is further limiting wherein the outlet port is approximately in the middle of the bottom wall.

Claim 46 is further limiting wherein the side walls taper inwardly to meet the outlet port.

Claim 47 is further limiting wherein the bottom wall is adjacent and substantially perpendicular to the two side wall portions.

Figures 1 and 2 on page 2563 of Goodey et al. illustrate these properties of the apparatus.

Claims 48 and 49 of the instant application are further limiting wherein the side walls taper to meet the inlet port and the angle formed is less than 90 degrees.

Figure 6-16 of Fogler illustrates a reactor with these tapering properties.

Claim 50 is further limiting wherein the geometry of the outlet port with respect to the bottom wall is described. Figures 1 and 2 of Goodey et al. illustrates a device with these properties.

Claim 56 is further limiting comprising an access channel in fluid communication with the inlet port.

Claim 57 is further limiting comprising a collection means in communication with the outlet port.

Figure 2A of Goodey et al. illustrates inlet and outlet pipes in communication with the inlet and output of the chamber.

Claim 58 is further limiting wherein flow of the sample is affected by flow through the device.

Figure 6-16 of Fogler illustrates such a reactor wherein the geometry of the reactor affects the flow through the reactor.

Claim 59 is further limiting wherein flow is effected using a pump.

Such a pump is described in column 1, middle paragraph of pages 2562 of Goodey et al.



Claim 60 is further limiting wherein the chamber comprises a variable volume. The dimensions of Figure 1A indicate a variable size of the outlet in the bottom wall of the chamber.

Claim 61 is further limiting wherein the substrate and the overlying cover and a recess are present. Claim 62 further limits the type of materials of the cover and substrate. Claim 63 and 76 are further limiting wherein the glass cover is bound to the substrate.

Figure 1 of Levesque et al. illustrates such a parallel plate channel flow device with a glass substrate attached to overlying glass cover, and a recess.

Claim 69 is further limiting wherein the device fragments biological fluids.

Claim 71 is further limiting comprising the analysis biological samples.

Claim 72 is further limiting comprising an assay kit for the analysis of biological samples.

Claim 73 is further limiting wherein the device is disposable.

Levesque et al. applies shear stresses to cellular solutions [see title and abstract of Levesque et al.] The device in Levesque et al. is disposable as it is capable of being disposed of.

Claim 74 is further limiting and is a method for fragmenting nucleic acids using the provided apparatus involving pumping a sample through the device and collecting the resultant fluids.

As described above, the instant combination of references teaches the device that executes the process of fragmenting nucleic acids in the instant claim.

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify fluid package interface of Goodey et al. by tapering the inlet of the reactor as illustrated in Fogler because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, the tapered reactor in Fogler is an alternative to the reactor of Goodey et al. There would have been a reasonable expectation of success in combining Goodey et al. with Fogler because both are reactor systems used for manipulating polymers. It would have been further obvious to modify devices of Goodey et al. and Fogler et al. by use of the cellular shearing device of Levesque et al. and the mechanical shearing of oligonucleotides in Costa et al. because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, substituting cells and nucleic acids as shown in Levesque et al. and Costa et al., respectively for the latex particles in Goodey et al. would have resulted in the predictable result of shearing of the nucleotides in the apparatus of Goodey et al. There would have been a reasonable expectation of success in combining the biological shearing devices of Levesque et al. and Costa et al.

with the reactors of Goodey et al. and Fogler because the apparatus of Goodey et al. is generally applicable to these biological solutions.

Response to Arguments:

Applicant's arguments filed 16 January 2009 have been fully considered but they are not persuasive.

In response to applicant's argument that Goodey et al. is nonanalogous art, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, applicant's arguments are not persuasive because both Goodey et al. and the instant application are drawn to reactor systems for shearing polymers (i.e. DNA is a type of biopolymer).

In response to applicant's argument that Goodey et al. and Fogler relate nonanalogous art (i.e. with respect to each other and the instant application), it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, both Goodey et al. and Fogler are analogous because they both relate to reactor systems for housing reactions. While applicant argues definitions for "microfabricated"

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from Wikipedia to differentiate large vs. small, these definitions are not recited in the instant claims or disclosed in the instant specification.

On page 13 of the Remarks, applicant continues to argue that there is no motivation or reasonable expectation of success in combining Goodey et al. with Fogler. It is noted that the rationale and reasonable expectation of success for combining Goodey et al and Fogler is stated above and reiterated below:

It would have been obvious to someone of ordinary skill in the art at the time of the instant invention to modify fluid package interface of Goodey et al. by tapering the inlet of the reactor as illustrated in Fogler because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, the tapered reactor in Fogler is an alternative to the reactor of Goodey et al. There would have been a reasonable expectation of success in combining Goodey et al. with Fogler because both are reactor systems uses for manipulating polymers.

In response to applicant's argument that Levesque et al. is nonanalogous art relative to Goodey et al., Fogler, and the instant application, it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed. Cir. 1992). In this case, it is noted that all of the prior art relates to reactor systems for the analysis of molecules. Specifically, the art of Levesque et al. is utilized to illustrate the effects of shear stress on cells. The combination of Levesque et al., Fogler, Goodey et al., (and Costa et al.) together teach all of the limitations of the instant set of claims with the rationale for combination, as discussed above.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #2:

Claim 42 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goodey et al. in view of Fogler in view of Levesque et al. in view of Costa et al. as applied to claims 40, 43-50, 56-63, 69, and 71-74 above, and further in view of Feichtinger [US Patent 3,356,489; issued 5 December 1967].

Claim 42 is further limiting wherein the fragmentation cell is generally pear shaped.

Goodey et al., Fogler, Levesque et al., and Costa et al. make obvious an apparatus for fragmenting oligonucleotides using a shearing force, as discussed above.

Goodey et al., Fogler, Levesque et al., and Costa et al. do not teach a pear shaped reactor.

The patent of Feichtinger illustrates a reactor for treating metallic melts that is essentially pear shaped (see cover figure).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the nucleic acid fragmentation device of Goodey et al., Fogler, Levesque et al., and Costa et al. by use of the pear shaped reactor in Feichtinger wherein the motivation would have been that a pear shaped reactor allows for better mixing [see figures in Feichtinger and column 1, lines 50-55].

Response to Arguments:

Applicant's arguments filed 16 January 2009 have been fully considered but they are not persuasive.

Applicant relies on the alleged deficiencies of 35 U.S.C. 103 Rejection #1 to argue with respect to the instant rejection. Since applicant's arguments are not persuasive, as discussed above, the instant rejection is maintained.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #3:

Claims 51-53, 70, and 75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodey et al. in view of Fogler in view of Levesque et al. in view of Costa et al. as applied to claims 40, 43-50, 56-63, 69, and 71-74 above, and further in view of Cottingham et al. [US Patent 5,783,148; issued 21 July 1998].

Claims 51-53 are further limiting wherein there is an obstacle in the cell that bifurcates flow of the liquid.

Claims 70 and 75 are further limiting wherein the fragmented nucleotides undergo amplification.

Goodey et al., Fogler, Levesque et al., and Costa et al. make obvious an apparatus for fragmenting oligonucleotides using a shearing force, as discussed above.

Goodey et al., Fogler, Levesque et al., and Costa et al. do not teach reactors with obstacles, nor do they teach amplification.

The invention of Cottingham et al. teaches a nucleic acid amplification method and apparatus.

The cover figure of the patent of Cottingham et al. illustrates a chamber with obstacles used to collect biological samples for amplification upon flow of the sample

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through the device. The obstacles (or wells) effect the flow of liquid through the reaction chamber in order to amplify the biological sample in the well.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the nucleic acid fragmentation device of Goodey et al., Fogler, Levesque et al., and Costa et al. by use of the in amplification device with wells (obstacles) in Cottingham et al. wherein the motivation would have been that this amplification device uses fluid flow to expedite and more fully decontaminate amplification reactions [see column 1, line 65, to column 2, line 3 of Cottingham et al.]

Response to Arguments:

Applicant's arguments filed 16 January 2009 have been fully considered but they are not persuasive.

Applicant relies on the alleged deficiencies of 35 U.S.C. 103 Rejection #1 to argue with respect to the instant rejection. Since applicant's arguments are not persuasive, as discussed above, the instant rejection is maintained.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #4:

Claim 54 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goodey et al. in view of Fogler in view of Levesque et al. in view of Costa et al. in view of Cottingham et al. as applied to claims 40, 43-53, 56-63, 69-70, and 71-75 above, and further in view of Raghu et al. [US Patent 5,853,624; issued 29 December 1998].

Claim 54 is further limiting in which the obstacle in generally triangular.

Goodey et al., Fogler, Levesque et al., Costa et al., and Cottingham et al. make obvious an apparatus for fragmenting oligonucleotides using a shearing force, as discussed above.

Goodey et al., Fogler, Levesque et al., Costa et al., and Cottingham et al. do not teach a reactor with a triangular obstacle.

The invention of Raghu et al. teaches a fluidic spray nozzle for use in cooling towers.

Figure 2 of Raghu et al. illustrates such a triangular nozzle affecting the flow of liquid through the nozzle.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the nucleic acid fragmentation device of Goodey et al., Fogler, Levesque et al., Costa et al., and Cottingham et al. by use of the triangular obstacle in Raghu et al. wherein the motivation would have been that this triangular device in Raghu et al. optimizes the flow through the nozzle [see Figures 2 and 4 of Raghu et al., and column 2, lines 45-50].

Response to Arguments:

Applicant's arguments filed 16 January 2009 have been fully considered but they are not persuasive.



Applicant relies on the alleged deficiencies of 35 U.S.C. 103 Rejection #1 to argue with respect to the instant rejection. Since applicant's arguments are not persuasive, as discussed above, the instant rejection is maintained.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #5:

Claims 64 and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodey et al. in view of Fogler in view of Levesque et al. in view of Costa et al. as applied to claims 40, 43-50, 56-63, 69, and 71-74 above, and further in view of Sprague et al. [Circulation, volume 3, pages 648-656, 1987].

Claims 64 and 66 are further limiting comprising a plurality of serially connected chambers.

Goodey et al., Fogler, Levesque et al., and Costa et al. make obvious an apparatus for fragmenting oligonucleotides using a shearing force, as discussed above.

Goodey et al., Fogler, Levesque et al., and Costa et al. do not teach a plurality of chambers.

The article of Sprague et al. studies the influence of a laminar steady state fluid imposed wall shear stress on the binding, internalization, and degradation of lipoproteins.

Specifically, the abstract of Sprague et al. indicates that the application of a shear stress to endothelial cells in two chambers in series.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the nucleic acid fragmentation device of Goodey et al., Fogler, Levesque et al., and Costa et al. by use of the serial reactor system in Sprague et al. wherein the motivation would have been that the serial reactor system has the advantage of having its properties varied at more points along the system with more conditions [see abstract and Figure 1 of Sprague et al.]

Response to Arguments:

Applicant's arguments filed 16 January 2009 have been fully considered but they are not persuasive.

Applicant relies on the alleged deficiencies of 35 U.S.C. 103 Rejection #1 to argue with respect to the instant rejection. Since applicant's arguments are not persuasive, as discussed above, the instant rejection is maintained.

The following rejection is reiterated:

35 U.S.C. 103 Rejection #6:

Claims 65 and 67-68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodey et al. in view of Fogler in view of Levesque et al. in view of Costa et al. in view of Sprague et al. as applied to claims 40, 43-50, 56-64, 66, 69, and 71-74 above, and further in view of Corominas [US PG PUB 2003/0089655 A1, published 15 May 2003; Filed, 5 October 2002].

Claim 65 is further limiting wherein there is a third fragmentation cell.

Claims 67-68 are further limiting wherein the size of the outlet port decreases sequentially along the fragmentation cell.

Goodey et al., Fogler, Levesque et al., Costa et al., and Sprague make obvious a serial apparatus for fragmenting oligonucleotides using a shearing force, as discussed above.

Goodey et al., Fogler, Levesque et al., Costa et al., and Sprague et al. do not teach a third chamber, or sequentially decreasing the size of the output.

Corominas teach a device for filtering fluid substances used for meat materials.

The device of Corominas flows a liquid through a plurality of chambers with continuously smaller filters (i.e. more than two chambers) for the purpose of filtering out continuously smaller particles [see cover figure of Corominas].

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the serial nucleic acid fragmentation device of Goodey et al., Fogler, Levesque et al., Costa et al., and Sprague et al. by use of the sequentially fine filtration system of Corominas wherein the motivation would have been that the device of Corominas has the advantage of resulting in a more homogeneous product as a result of continuously finer filters [see cover figure and abstract of Corominas].

The following rejection is newly applied and necessitated by applicant's amendments:

35 U.S.C. 103 Rejection #7:

Claim 77 is rejected under 35 U.S.C. 103(a) as being unpatentable over Goodey et al. in view of Fogler in view of Levesque et al. in view of Costa et al. as applied to

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claims 40, 43-50, 56-63, 69, and 71-74 above, and further in view of Pfahler [Doctoral Dissertation, University of Pennsylvania, 1992].

Goodey et al., Fogler, Levesque et al., and Costa et al. make obvious an apparatus for fragmenting oligonucleotides using a shearing force, as discussed above.

Goodey et al., Fogler, Levesque et al., and Costa et al. do not teach a channel with the constriction width between 5 and 50  $\mu\text{m}$ .

The dissertation of Pfahler studies liquid transportation in micron and submicron size channels. Specifically, page 81 of Pfahler illustrates such a dimensioned constriction.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to modify the nucleic acid fragmentation device of Goodey et al., Fogler, Levesque et al., and Costa et al. by use of the recited dimensioned constriction in Pfahler because it is obvious to substitute known elements in the prior art to yield a predictable result. In this instance, the narrower constriction on Pfahler provides an alternate form of constriction as in Goodey et al. There would have been a reasonable expectation of success in combining Pfahler with Goodey et al., Fogler, Levesque et al., and Costa et al. because all of the sources pertain to analogous reactor systems for analyzing polymers or biopolymers.

### ***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Marjorie Moran, Supervisory Patent Examiner, can be reached at (571) 272-0720.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information on the PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/RSN/  
Russell S. Negin  
11 April 2009

/Marjorie Moran/  
Supervisory Patent Examiner, Art Unit 1631